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Evaluation of the Clinical Efficacy of Empagliflozin Combined with Levosimendan in the Treatment of Patients with Coronary Heart Disease and Heart Failure

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Abstract: *Objective:* To explore the effectiveness of empagliflozin + levosimendan in the treatment of coronary heart disease and heart failure. *Methods:* 78 patients with coronary heart disease and heart failure who visited the hospital from August 2024 to August 2025 were selected and divided into groups using a random number table, with 39 cases in each group. The control group received levosimendan treatment, and the observation group received empagliflozin combined with levosimendan treatment. The efficacy of the two groups was compared. *Results:* After completing treatment, the cardiac output and left ventricular ejection fraction of the observation group were higher than those of the control group, and the level of N-terminal pro-B-type natriuretic peptide was significantly lower ($P < 0.05$); the six-minute walking distance of the observation group was longer than that of the control group, and their exercise tolerance was better ($P < 0.05$); *Observation:* The tumor necrosis factor-α, high-sensitivity C-reactive protein, interleukin-1β, type I collagen, connective tissue growth factor, and α-smooth muscle actin in the group were lower than those in the control group ($P < 0.05$); the total incidence of adverse reactions was compared between the two groups ($P > 0.05$). *Conclusion:* Empagliflozin combined with levosimendan in the treatment of coronary heart disease and heart failure can improve cardiac function, reduce inflammation, delay myocardial fibrosis, and improve exercise tolerance, with good safety.

Keywords: Coronary heart disease; Heart Failure; Empagliflozin; Levosimendan

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1. Introduction

Coronary heart disease is a common cardiovascular disease in clinical practice. When the disease develops to an advanced stage, it will mostly progress to heart failure [1]. Levosimendan is a new type of calcium-sensitizing drug used clinically, which can enhance myocardial contractility and exert a positive inotropic

regulating effect [2]. Levosimendan can effectively expand coronary arteries and systemic peripheral blood vessels, reduce the preload and afterload of the heart, and improve the blood and oxygen supply of the heart [3]. However, it is difficult to completely improve the long-term prognosis of patients using levosimendan alone. Empagliflozin works through multiple mechanisms. This study will focus on analyzing the clinical effects and drug safety of empagliflozin combined with levosimendan in the treatment of patients with coronary heart disease and heart failure. The study selected 78 patients with coronary heart disease and heart failure admitted to the hospital as subjects, aiming to explore more efficient combined treatment options for patients with coronary heart disease and heart failure.

2. Materials and methods

2.1. Baseline data

78 patients with coronary heart disease and heart failure were selected in the hospital, all of whom were treated between August 2024 and August 2025. The patients were grouped according to the random number table method. Among the 39 cases in the control group, 17 were female and 22 were male; the age range was 57 to 90 years old, with an average of (68.79 ± 6.85) years; the disease duration ranged from 1 to 6 years, with an average of (3.89 ± 0.42) years; NYHA classification included 18 cases of grade II, 12 cases of grade III, and 9 cases of grade IV. Among the 39 cases in the observation group, 15 were female and 24 were male; the age range was 58 to 92 years old, with an average of (68.46 ± 6.54) years; the disease duration ranged from 1 to 7 years, with an average of (3.85 ± 0.40) years; NYNA classification included 17 cases of grade II, 11 cases of grade III, and 11 cases of grade IV. Comparison of the data between the two groups ($P > 0.05$).

Inclusion criteria: (1) Meet the diagnostic criteria for coronary heart disease and heart failure; (2) NYHA cardiac function class II to IV; (3) Left ventricular ejection fraction less than 50%; (4) Patients and their families gave informed consent and signed an informed consent form.

Exclusion criteria: (1) Those with acute myocardial infarction, cardiogenic shock, or severe arrhythmia; (2) Those who are allergic to the drugs in this study or have contraindications.

2.2. Method

The control group was treated with levosimendan (Chengdu Xinhengchuang Pharmaceutical Co., Ltd., national drug approval number H20243485, 5ml: 12.5mg*1 bottle*4 boxes), with an initial dose of 12 μg/kg, slowly intravenously injected within 10 minutes, and then continued intravenous pumping at 0.1 μg/(kg·min) for 24 hours.

The observation group was treated with empagliflozin (Sichuan Kelun Pharmaceutical Co., Ltd., national drug approval number H20203411, 10 mg*14 tablets) combined with levosimendan. On the basis of the control group, empagliflozin 10 mg was taken orally once a day for 7 consecutive days.

2.3. Observation indicators

(1) Cardiac function indicators (cardiac output, left ventricular ejection fraction) and heart failure marker indicators (N-terminal pro-B-type natriuretic peptide) before treatment and 7 days after treatment.
(2) Six-minute walking distance before treatment and 7 days after treatment.
(3) Tumor necrosis factor-α, high-sensitivity C-reactive protein, and interleukin-1β before treatment and 7 days after treatment.

(4) Myocardial fibrosis indicators before treatment and after 7 days of treatment. Including collagen I, connective tissue growth factor, and α-smooth muscle actin.

(5) Statistics of adverse reactions that occurred during treatment in both groups, including dizziness, headache, tachycardia, nausea, and hypotension.

2.4. Statistical processing

Data were processed with SPSS 26.0; count data were expressed as (%), and the chi-square test was used for differences. Mean ± SD was used to represent measurement data, and a *t*-test was used. ($P < 0.05$) indicates that the difference is statistically significant.

3. Results

3.1. Comparison of cardiac function indicators and heart failure markers

As shown in **Table 1**, the comparison of cardiac function and heart failure marker indicators between the two groups before treatment ($P > 0.05$); after treatment, the cardiac output and left ventricular ejection fraction of the observation group were higher than those of the control group, and the N-terminal pro-B-type natriuretic peptide was lower than that of the control group ($P < 0.05$).

Table 1. Comparison of cardiac function and heart failure markers (Mean ± SD)

Group	Cardiac output (L/min)		Left ventricular ejection fraction (%)		N-terminal pro-B-type natriuretic peptide (pg/ml)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n = 39)	3.05 ± 0.44	4.62 ± 0.52	43.98 ± 6.52	55.63 ± 6.14	950.65 ± 89.25	192.65 ± 30.05
Control group (n = 39)	3.07 ± 0.42	3.90 ± 0.62	43.77 ± 7.05	48.88 ± 5.42	951.42 ± 85.79	300.15 ± 28.42
t	0.2053	5.5566	0.1365	5.1469	0.0388	16.2313
P	0.8379	< 0.0001	0.8917	< 0.0001	0.9691	< 0.0001

3.2. Comparison of six-minute walking distance

As shown in **Table 2**, the six-minute walking distance of the two groups before treatment was compared ($P > 0.05$); the six-minute walking distance of the observation group after treatment was longer than that of the control group ($P < 0.05$).

Table 2. Comparison of six-minute walking distance (Mean ± SD, m)

Group	Before treatment	After treatment
Observation group (n = 39)	289.65 ± 35.98	405.93 ± 28.79
Control group (n = 39)	290.45 ± 36.15	308.79 ± 22.77
t	0.0979	16.5269
P	0.9222	< 0.0001

3.3. Comparison of inflammation indicators

As shown in **Table 3**, there was no significant difference in the levels of inflammatory indicators between

the two groups before treatment ($P > 0.05$); after treatment, the observation group was lower than the control group ($P < 0.05$).

Table 3. Comparison of inflammation indicators (Mean ± SD)

Group	Tumor necrosis factor-α (ng/L)		High-sensitivity C-reactive protein (mg/L)		Interleukin-1β (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n = 39)	1.88 ± 0.31	0.85 ± 0.15	4.31 ± 0.52	1.55 ± 0.20	36.79 ± 8.12	18.21 ± 2.65
Control group (n = 39)	1.89 ± 0.29	1.08 ± 0.20	4.29 ± 0.61	1.92 ± 0.27	36.80 ± 8.42	20.93 ± 3.12
t	0.1471	5.7453	0.1558	6.8768	0.0053	4.1495
P	0.8834	< 0.0001	0.8766	< 0.0001	0.9958	0.0001

3.4. Comparison of myocardial fibrosis indicators

As shown in **Table 4**, there was no significant difference in myocardial fibrosis indicators between the two groups of patients before treatment ($P > 0.05$); after treatment, the indicators in the observation group were lower than those in the control group ($P < 0.05$).

Table 4. Comparison of myocardial fibrosis indicators (Mean ± SD, μg/L)

Group	Collagen I		Connective tissue growth factor		α-smooth muscle actin	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n = 39)	230.55 ± 25.93	162.52 ± 23.78	213.56 ± 25.97	114.82 ± 13.05	143.65 ± 25.93	90.56 ± 15.11
Control group (n = 39)	229.78 ± 26.12	190.53 ± 22.05	214.05 ± 23.82	125.93 ± 20.45	142.79 ± 27.05	102.65 ± 18.86
t	0.1306	5.3938	0.0868	2.8600	0.1433	3.1242
P	0.8964	< 0.0001	0.9310	0.0055	0.8864	0.0025

3.5. Comparison of treatment safety

As shown in **Table 5**, there was no significant difference in the total incidence of adverse reactions between the two groups ($P > 0.05$).

Table 5. Treatment safety comparison [n (%)]

Group	(n)	Dizziness and headache	Tachycardia	Disgusting	Hypotension	Total
Observation group	39	2(5.13)	1(2.56)	1(2.56)	1(2.56)	5(12.82)
Control group	39	1(2.56)	1(2.56)	1(2.56)	1(2.56)	4(10.26)
x^2	-	-	-	-	-	0.1256
P	-	-	-	-	-	0.7230

4. Discussion

Patients with coronary heart disease and heart failure are routinely treated with levosimendan and combined with empagliflozin for intervention. The action pathways of the two drugs are independent of each other and highly complementary, and can better improve the prognosis [4–5].

The data of this study showed that the cardiac output and left ventricular ejection fraction of the observation group increased, and the N-terminal pro-B-type natriuretic peptide decreased, compared with the control group ($P < 0.05$). This shows that the combined intervention of the two drugs is more effective in improving the patient's blood pumping function. Levosimendan can quickly increase myocardial contractility and improve the patient's cardiac systolic function in the short term. Empagliflozin continues to improve cardiac function through a variety of ways, that is, improving myocardial energy metabolism efficiency, reducing cardiac preload and afterload, promoting the excretion of sodium ions and water in the body, and reducing cardiac capacity load [6]. The combined use of the two drugs can significantly improve myocardial contractility, enhance the heart's pumping function, while reducing the pressure on the ventricular wall and reducing the overall load on the ventricle. It can be seen from the results that the six-minute walking distance of the observation group was longer than that of the control group. The significant improvement in the patient's exercise tolerance after combined medication is due to the combined effects of all aspects. The effective recovery of cardiac function ensures normal perfusion of systemic blood circulation and improves the blood and oxygen supply levels of peripheral circulation. At the level of regulating inflammation in the body, the inhibitory effect of various inflammatory factors such as tumor necrosis factor-α, high-sensitivity C-reactive protein, and interleukin-1β in the observation group was far better than that of levosimendan alone ($P < 0.05$). After analysis, empagliflozin can reduce the secretion and expression of various pro-inflammatory cytokines and exert a stable anti-inflammatory effect. The significant improvement in inflammatory indicators in patients after combined treatment fully demonstrates that empagliflozin can effectively make up for the deficiencies of levosimendan in anti-inflammatory regulation, effectively reduce local and systemic inflammatory damage to the myocardium, and repair damaged cardiomyocytes [7]. Myocardial fibrosis is the core link that promotes the continued progression of heart failure [8]. After treatment, the levels of type I collagen, connective tissue growth factor, and α-smooth muscle actin in the observation group were lower than those in the control group ($P < 0.05$). This shows that the combined drug regimen can inhibit and delay the development of myocardial fibrosis. In terms of treatment safety, there was no significant statistical difference between the two groups ($P > 0.05$). This shows that combining levosimendan with empagliflozin on the basis of conventional treatment will not increase the patient's treatment safety risks.

In summary, empagliflozin combined with levosimendan is effective in treating coronary heart disease and heart failure. It can improve sexual function, reduce inflammatory response, delay the process of myocardial fibrosis, improve exercise tolerance, and has good safety.

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Disclosure statement

The author declares no conflict of interest.

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